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Regarding "A prospective study of ultrasound-guided thrombin injection of femoral pseudoaneurysm: A trend toward minimal medication"

It is with interest I read the article by Olsen et al.[1] Their data support the findings that lower doses of thrombin are effective for treatment of femoral pseudoaneurysm, as previously reported by Reeder et al.[2]

However, there appear to be troublesome omissions with regard to their methods. In this prospective study there is no mention of adherence to the principles of the Declaration of Helsinki.[3] Point 13 of the Declaration states that "The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence." The *Journal of Vascular Surgery* publication rules stipulate that "Manuscripts that involve research conducted on human subjects must follow the principles outlined in the Declaration of Helsinki and include a statement in the Methods section that the experimental protocol and informed consent were approved by the institutional review board and that all subjects gave informed consent." In the article by Olsen and colleagues, no mention is made of informed patient consent or of institutional review board approval, again, required of all studies involving human research.[4] Adherence to these rules is mandatory to ensure the highest ethical standards when conducting biomedical research.

In addition, while exclusion criteria were given, no mention was made regarding the number of patients excluded from the study. Did any eligible patients refuse participation in the study? Were any eligible patients not included in the study for any other reason?

Prospective study designs require that informed consent be obtained, institutional review board approval be obtained, and study end points be defined before patient enrollment in a study. Olsen and colleagues do not provide enough information in their article to determine whether these rules were followed. One could suppose that the patients treated in their study would have been treated similarly in the absence of a defined protocol, and thus informed consent for participation in a trial was unnecessary because their treatment conformed to standard of care. If so, this study should then be more appropriately called a retrospective analysis, not a prospective study.

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Reply

We appreciate your comments, and we hope this will clarify your concerns. This was not an "experimental procedure involving human subjects." This method of treatment of common femoral pseudoaneurysm is our standard practice, as it is in many other centers. In our practice, ultrasound-guided thrombin injection is attempted, and if it is unsuccessful, a second attempt is made. If the second attempt fails, surgical repair is implemented. Please note that treatment options including compression, open surgical repair, and thrombin injection were discussed with each patient. In addition, risks and benefits of each intervention were discussed.

You are correct in stating that the institutional review board must approve the off-label use of a drug if its use involves human subjects and you are researching its effect. The board is not required to review off-label use of a drug if "it is intended to be solely the practice of medicine," which it was in our case. This is our standard practice for treating pseudoaneurysm. As the data were reviewed, it was evident that less thrombin was necessary to successfully thrombose a pseudoaneurysm. Perhaps a better prospective study would be to establish a dilution and administer a single amount, and determine if that would cause thrombosis, rather than report a trend.

During the study period, 2 patients were considered "outliers." One patient with a pseudoaneurysm less than 2.0 cm chose compression therapy. This was successful, but required two intervals of compression. The other patient, with a pseudoaneurysm greater than 8 cm, underwent successful ultrasound-guided thrombin injection. This patient would have undergone open surgical repair if only the size of the pseudoaneurysm was considered. However, the cardiologist believed she was at high-risk for anesthesia and surgery. Neither of these patients was included in the study.

If a prospective study requires that we must establish different dosing schedules before initiation of the study, rather than prospectively gather data, documenting the dosage used in each case, then we lack this variable. The data were gathered prospectively and reviewed retrospectively. We have a database established for our various procedures. If one of us chose to follow the outcomes of a procedure, there is the option to retrospectively review previous cases or begin following up all patients treated during a certain period. If a prospective study requires that last factor, then you are correct in deeming this a retrospective study.

Thank you for you comments.

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